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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,732	08/16/2001	Bob D. Brown	OASBIO.001C1	4615

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/931,732	BROWN ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133) Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2006 and 21 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 21-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 21-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5-9-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on March 6, 2006 and June 21, 2006.

Currently, claims 1-12 and 21-48 are pending. Applicants have cancelled claims 13-20 and made election **without traverse** of claims 1-12 and 21-48 pertaining to Bcl-2 in the reply filed on June 21, 2006. Accordingly, inventions Bcl-2a, Bcl-2b, Bcl-2c, Bcl-xl, protein kinase Cα, protein kinase Cθ, and protein kinase Cδ are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 112

Claims 1-12 and 21-34 remain rejected under 35 U.S.C. 112, first paragraph, as failed to comply with the written description requirement for the reasons of record as set forth in the Office action mailed on November 4, 2005 and for the reasons stated below.

The claims are drawn to antisense oligonucleotides between 6-50 bases in length comprising one or more non-natural bases substituting for one or more natural bases that are positioned and aligned with a single nucleotide polymorphism in the RNA target region. The specification, claims, and the art do not adequately describe the distinguishing features shared by the broad genera comprising targeting any type of genes with any number of single nucleotide polymorphisms represented by non-natural bases in the instantly claimed antisense oligonucleotides.

Applicant's arguments filed on March 6, 2006 have been fully considered but they are not persuasive.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and /or chemical properties, functional characteristics, structure/function correlation, or any combination thereof. Although the instant specification discloses a list of potential antisense oligonucleotides (page 10) and some specific antisense oligonucleotide sequences for PKC-α (page 14) and bcl-2 (pages 15 and 18), the oligonucleotides disclosed therein are not representative of the genera as claimed in claims 1-12 and 21-34. As broadly claimed, the specification does not clearly allow persons of

ordinary skill in the art to recognize that the inventors invented what is claimed in claims 1-12 and 21-34. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991), which clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (see page 1117). Since claims 1-12 and 21-34 claim both disclosed and undisclosed (or unidentified) antisense oligonucleotides, adequate written description requires more than a countable number of antisense oligonucleotides as provided in the specification.

Corollary to the instant claims to broad genera of antisense oligonucleotides in claims 1-12 and 21-34, in *Fiddes,* claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class since the specification provided only the bovine sequence (See *Fiddes v. Baird,* 30 USPQ2nd 1481 at 1483).

Claim Rejections - 35 USC § 102(b)/103(a)

Claims 1-6 and 21-25 stand rejected under 35 U.S.C. 102(b) or 35 USC 103(a) as being anticipated by or obvious over Bergstrom et al. (U.S. Patent 5,681,947, also Reference 22, PTO Form 1449 filed on August 28, 2002) for the reasons of record as set forth in the Office action mailed on November 4, 2005 and for the reasons stated below.

The claims are drawn to antisense oligonucleotides comprising substitution of one or more naturally occurring bases with one or more non-naturally occurring bases (including 3-nitropyrrole) that align with a single nucleotide polymorphism position in the target region of

RNA molecules and wherein said antisense oligonucleotides comprise RNase H recruiting region.

Applicant's arguments filed on March 6, 2006 have been fully considered but they are not persuasive. Applicant asserts that the Bergstrom et al. patent does not teach or suggest antisense oligonucleotides directed to SNPs but instead teaches antisense oligonucleotides that are directed to nucleic acid target sequences with "significant variability". Applicant repeatedly asserts that the instantly claimed invention is not anticipated by or obvious over Bergstrom et al., because the applicant' invention is an antisense oligonucleotide that targets RNAs containing one or more SNPs while the antisense oligonucleotide of Bergstrom et al., targets RNAs with "significant variability", thereby Bergstrom et al. teach away from the instantly claimed invention. The definition of SNP as well as what is entailed in SNPs are described in Brookes' review article (*Gene*, 1999, 234:177-186). See the attached citation. On page 177, SNPs are defined as single base pair positions in genomic DNA at which different sequence alternatives (alleles) exist in normal individuals in some populations. On page 178, it is clearly stated that SNPs entail varying degrees of nucleotide base substitutions and that there are several million single base differences between any two individuals. Further, as claimed, the instant claims are directed to "**one or more** SNPs", which are indistinguishable from the oligonucleotides of Bergstrom et al.

Bergstrom et al. expressly teach synthetic oligonucleotides containing as many as 9 natural DNA bases including a CG dinucleotide are replaced by 3-nitropyrrole deoxyribonucleoside in a 17-mer (column 7, lines 43-46 and Table 1, line 23, Primer No. 83), which indicates that the universal or degenerate bases comprise no more than about 50% of the 17 base-long oligonucleotide. Bergstrom et al. also disclose modified oligonucleotides

containing one (Primer Nos. 73 and 75), three (Primer No. 77), four (Primer No. 72), and six (Primer No. 78) 3-nitropyrrole universal bases, which comprise less than 50% of the oligonucleotides. Bergstrom et al. further teach that the use of a universal nucleoside at the degenerate sites can be widely applied to different applications including antisense oligonucleotide therapeutics or a genetic probe for detecting mutations in various assays (column 8, lines 40-65). Moreover, Bergstrom et al. teach oligonucleotides comprising at least 10 nucleosides, wherein at least one nucleoside is a universal nucleoside. Bergstrom et al. teach that this incorporation of one or more universal nucleosides into the oligomer makes bonding to unknown bases possible and allows the oligonucleotide to match ambiguous or unknown nucleic acid sequences (see Figures 1 and 4, columns 2-3, lines 67-4, and column 4, lines 13-16).

It is unclear how Applicant can arrive at the assumption that Bergstrom et al. do not anticipate the structural limitations of the antisense oligonucleotide between 6 and 50 bases in length comprising one or more natural bases are replaced by one or more non-naturally occurring bases (known as universal bases) such as Bergstrom et al's 3-nitropyrrole, wherein said universal bases comprise no more than about 50%. In particular, Applicant has failed to provide any evidence contrary to the prior art teachings of Bergstrom et al. Applicant's argument that the term "antisense oligonucleotide" appears only once in the Bergstrom et al's patent is irrelevant, since it is art-recognized knowledge that a synthetic oligonucleotide for a sequencing primer or a hybridization probe is designed in the antisense orientation in order for it to hybridize to the target nucleic acid sequence. Thus, even if Bergstrom et al. does not disclose the term "antisense oligonucleotide" in their patent, it should be self-evident that the disclosure of primer sequences containing universal bases satisfy the structural limitations recited in claims 1-2 and 21 because

the universal bases of an oligonucleotide used as a sequencing primer or a hybridization probe align with the degenerate positions of target DNA or RNA sequences as taught by Bergstrom et al. (see column 2, lines 60-64).

Rejections necessitated by amendment

The following rejections are new rejections applied to the instant application.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to improved antisense oligonucleotides/ribozymes targeted to bcl-2 comprising one or more non-natural bases substituting for one or more natural bases that are positioned and aligned with a single nucleotide polymorphism in the RNA target region, wherein the improvement further comprises RNase H, RNase L, and RNase P recruiting regions.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and /or chemical properties,

functional characteristics, structure/function correlation, or any combination thereof. In the instant case, the specification discloses Figure 3, which illustrates that two different alleles of bcl-2 gene, known as bcl-2B and bcl-2C, are targeted with antisense oligonucleotides containing one or more universal bases, which appear to be represented by SEQ ID NOs: 26, 28, and 30 (page 18). The instant specification also discloses SEQ ID NO: 19 on page 15, which is described to be a bcl-2-targeted antisense molecule containing 7 universal bases. However, since the instant claims are drawn to any bcl-2 antisense oligonucleotides/ribozymes, adequate written description requires more than the species provided in the specification. Therefore, it is concluded that the 4 bcl-2-targeted antisense oligonucleotides (SEQ ID NOs: 19, 26, 28, and 30) are not representative of the genus encompassed by the broadly claimed bcl-2 antisense oligonucleotides.

Further, claims 43-46 are drawn to bcl-2 antisense oligonucleotides further comprising RNase L or RNase P recruiting regions and claims 47-48 are drawn to bcl-2 ribozymes. The instant specification provides no distinguishing identifying characteristics for these claimed subject matter since not even a single representative species for the claimed invention in claims 43-48 is disclosed in the instant specification.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991), which clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (see page 1117).

Since the instant specification does not provide adequate description of the instantly claimed bcl-2 antisense oligonucleotides and ribozymes and since the instant claims do not recite any specific SEQ ID NOs in reference to the bcl-2 antisense oligonucleotides or ribozymes, one skilled in the art would not be able to ascertain whether the inventor was in possession of the instantly claimed invention at the time the invention was made.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 37-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Riley et al. (US 6,518,017 B1, applicant's citation No. 2 of PTO/SB/08 filed on May 9, 2006).

The applied reference has a common assignee and two inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 37-42 are drawn to an antisense oligonucleotide comprising substitution of one or more naturally occurring bases with one or more non-naturally occurring bases that align with a single nucleotide polymorphism position in the target region of RNA molecules that encode a human oncogene, wherein said oncogene is Bcl-2 and said antisense oligonucleotide comprises a RNase H recruiting region.

Riley et al. disclose a bcl-2 antisense oligonucleotide (identified as 1063 or SEQ ID NO:48) comprising an RNase H-substrate region at the 5' end and 2 universal bases which can be selected from deoxy 5-nitroindole, deoxy 3-nitropyrrole, and deoxy inosine (column 7, lines 58-64; column 27, Example 9). The bcl-2 antisense oligonucleotide of Riley et al. would be expected to align with SNP positions in the bcl-2 target region since the bcl-2 antisense oligonucleotide of Riley et al. meet all of the structural requirements of the antisense oligonucleotides recited in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 37-44 and 47-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Riley et al (US 6,518,017 B1) as applied to claims 37-42 for §102(e) rejections above.

Claims 37-42 are described above.

Claims 43-44 are drawn to antisense oligonucleotides targeting bcl-2 gene, wherein said antisense oligonucleotides comprise less than 50% of universal bases that align with SNP positions and further comprise an RNase L recruiting region.

Claims 47-48 are drawn to ribozymes comprising an RNA target region and one or more universal bases, wherein the RNA target is bcl-2.

Riley et al. teach bcl-2 antisense oligonucleotides (column 27) and a method of producing antisense oligonucleotides useful for recruiting RNase L comprising a 2'-5' adenosine oligomer (column 14, lines 61-67). They also teach a repertoire of universal bases that can functionally substitute natural bases (columns 7-10). They teach a ribozyme structure consisting of an anchor, a cleaver, and a target RNA (Figure 3). They further teach that ribozyme is an oligonucleotide or oligonucleotide analog capable of catalytically cleaving a polynucleotide (column 4, lines 1-3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make bcl-2 antisense oligonucleotides/ribozymes comprising one or more universal bases and wherein said antisense oligonucleotides further comprise either RNase H or RNAse L recruiting region as taught by Riley et al. One of ordinary skill in the art would have been

motivated to utilize the teachings of Riley et al. in making bcl-2 antisense oligonucleotides and ribozymes as recited in the claims with a reasonable expectation of success, because bcl-2 antisense oligonucleotides with one or more universal bases and an RNase H recruiting region was already taught by Riley et al. (column 27) and because Riley et al. clearly teach the use of modified antisense oligonucleotides with universal bases comprising an RNase L recruiting region as well as ribozymes that are functionally equivalent to antisense oligonucleotides (column 4). Accordingly, the invention as a whole would therefore have been *prima facie* obvious to one skilled in the art at the time the invention was made.

Claims 37-40 and 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blood Weekly (*Antisense Technology: Patent Claims Allowed for Therapy Targeted Against Apoptosis Gene,* November 18, 1996, pages 6-7) in view of Torrence et al. (US 5,583,032, applicant's citation No. 15 of PTO-1449 filed on August 28, 2002) and Loakes et al. (*Nucleic Acids Research,* 1994, also applicants' citation No.7 of PTO/SB/O8 filed on May 9, 2006).

Blood Weekly teaches an antisense molecule targeted against the bcl-2 gene, which is named "G3139" by Genta Inc. It teaches that bcl-2 has been recognized as a significant factor in a number of human cancers and that preclinical experiments using G3139 has shown anti-tumor activity in animal models of various cancer types. Blood Weekly does not teach bcl-2 antisense oligonucleotides comprising an RNase L recruiting region and one or more universal bases.

Torrence et al. teach antisense oligonucleotides comprising RNase L recruiting regions, which specifically hybridize with 10-30 nucleotides of the respiratory syncytial virus (RSV) sequence (columns 1-2). They show that these antisense oligonucleotides successfully inhibit

RSV replication in previously infected human tracheal epithelial cells *in vitro* (columns 15-16, Example 8).

Loakes et al. teach an antisense oligonucleotide of 17 bases in length, wherein a single substitution of 5-nitroindole aligns with 4 different natural bases (A, T, G, C). Loakes et al. further teach that this modified oligonucleotide forms a stable duplex with a complementary strand containing natural bases, which indicates that 5-nitroindole behaves as universal nucleoside. They also teach that up to six substitutions of 5-nitroindole nucleosides are incorporated into the oligonucleotide strand (pages 4042-4043, also see Tables 1-2). They teach that the universal nucleobase 5-nitroindole can be used as primers for PCR and sequencing. It is an art-recognized knowledge that primers in PCR and sequencing comprise antisense oligonucleotides that hybridize with the target sequence. Although Loakes et al. do not explicitly teach that their modified oligonucleotide hybridizes with an mRNA molecule, the modified antisense of Loakes et al. will be able to hybridize with one or two more mRNA molecules because it is an art-recognized knowledge that nucleic acid oligonucleotides used for PCR or sequencing primers hybridize with mRNA sequences.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a bcl-2 antisense oligonucleotide with an RNase L recruiting region of Torrence et al. and one or more universal bases of Loakes et al. One of ordinary skill in the art would have been motivated to make such modifications to the bcl-2 antisense oligonucleotide of Blood Weekly, because Torrence et al. teach that an RNase L antisense oligonucleotide effectively inhibits the target gene expression in cells and because Loakes et al. teach that modified antisense oligonucleotides comprising universal bases do align with natural bases and

hybridize with a target gene sequence. Thus, the skilled artisan would have been motivated, with a reasonable expectation of success, to combine the teachings of the prior art to make a modified bcl-2 antisense oligonucleotide that is able to hybridize with different alleles of bcl-2 oncogene and effectively inhibit the bcl-2 expression in cells because it was an art-recognized goal to inhibit the expression of bcl-2 in cancer cells with a sequence-specific antisense oligonucleotide and apply such bcl-2 antisense oligonucleotides in clinical milieu as taught by Blood Weekly. Hence, the skilled artisan would have clearly contemplated to make a versatile and efficacious bcl-2 antisense oligonucleotide by combining the teachings of the above references. Accordingly, the invention taken as a whole is *prima facie* obvious.

Claims 37-42 and 45-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reed (US 5,831,066) in view of Krupp (*Biochimie,* 1993, applicant's citation No. 82 of PTO-1449 filed on August 28, 2002) and Loakes et al. (*Nucleic Acids Research,* 1994) as applied to claims 37-40 and 43-44 above.

Claims 37-42 and 45-46 are drawn to antisense oligonucleotides between 6-50 bases in length that comprise RNase H or RNase P recruiting region and non-naturally occurring bases in place of naturally occurring bases, which align with single nucleotide polymorphism positions in the Bcl-2 gene sequence.

Reed teaches the Bcl-2 antisense oligonucleotides between 7-20 nucleotides in length that specifically target a nucleic acid encoding Bcl-2, thereby inhibiting the Bcl2 expression *in vitro* in tumor cells (column 6, lines 45-64, Table 1, Examples 1-18). Reed does not teach the Bcl-2

antisense oligonucleotides comprise an RNase P recruiting region and non-naturally occurring bases in place of naturally occurring bases.

The reference of Krupp teaches that short antisense oligonucleotides are substrates for RNase H, therefore, are recognized and cleaved by RNase H (page 136). It teaches that both short and long antisense oligonucleotides are substrates for RNase P and that it is attractive to use a larger antisense RNA which contains an internal sequence for directing RNase P cleavage because RNase P harbors sequence specificity due to its property to target a perfectly base-paired sequence (pages 136-139).

The teachings of Loakes et al. are described above. See pages 14-15.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a bcl-2 antisense oligonucleotide comprising an RNase P recruiting region as taught by Krupp and further comprising one or more universal bases as taught by Loakes et al. One of ordinary skill in the art would have been motivated to modify the bcl-2 antisense oligonucleotide of Reed in view of the teachings of Krupp and Loakes et al. because Krupp teaches the versatility and specificity imparted by RNase P in antisense oligonucleotides and because Loakes et al. teach that modified antisense oligonucleotides comprising universal bases do align with natural bases and hybridize with a target gene sequence. Thus, the skilled artisan would have been motivated, with a reasonable expectation of success, to combine the teachings of the prior art to make a modified bcl-2 antisense oligonucleotide that is able to hybridize with different alleles of bcl-2 oncogene and effectively inhibit the bcl-2 expression in tumor cells because it was an art-recognized goal to inhibit the expression of bcl-2 in tumor cells with a sequence-specific antisense oligonucleotide as taught by Reed. Hence, the skilled artisan would

have clearly contemplated to make a versatile and efficacious bcl-2 antisense oligonucleotide by combining the teachings of the above references. Accordingly, the invention taken as a whole is *prima facie* obvious.

Double Patenting - Provisional

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

Claims 1-2, 23, 29, and 35-36 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 13-17, and 19 of copending Application No. 10/375,504. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. Claims 1-2, 23, 29, 35-36 of this application conflict with claims 1-10, 13-17, and 19 of Application No. 10/375,504.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of the conflicting claims are directed to oligonucleotides between about 10 and about 50 bases in length, wherein one or more bases are universal bases (also known as non-naturally occurring bases) selected from the group consisting of 2-deoxyinosine (equivalent to inosine base), 5-nitroindole, 3-nitropyrrole, and 2-deoxynebularine that comprise more than about 20-30% (equivalent to no more than about 50%), wherein said oligonucleotides

comprising said universal bases have decreased or increased affinity for a target (equivalent to hybridizing to two or more RNA molecules that differ in sequence by one or more SNP in the target regions that hybridize to said oligonucleotide. See the following paragraph for reasons).

In the instant case, claims 1-2, 23, 29, and 35-36 of the instant application contain a recitation of the intended use of the claimed invention :"...wherein said antisense oligonucleotide is able to hybridize...." (See lines 5-10 of claim 1 as well as lines 1-6 of claim 36), which must result in a structural difference between the claimed invention and the claimed invention of claims 1-10, 13-17, and 19 of Application No. 10/375,504 in order to patentably distinguish the claimed invention from the conflicting claims of copending Application No. 10/375,504. If the structure of the oligonucleotide of claims 1-10, 13-17, and 19 of the copending Application No. 10/375,504 is capable of performing the intended use, then it reads on the instantly claimed invention of claims 1-2, 23, 29, and 35-36, in the absence of evidence to the contrary. Accordingly, claims 1-2, 23, 29, 35-36 of this application conflict with claims 1-10, 13-17, and 19 of Application No. 10/375,504 due to the lack of patentable distinctness between the inventions in the two applications.

37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

TC1600
JANE ZARA, PH.D.
PRIMARY EXAMINER

Dana Shin
August 30, 2006